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Efficacy of High Sensitivity C- Reactive Protein, Lipoprotein A and Troponin I levels in Predicting Cardiovascular Disease Severity on Coronary Angiogram- A Prospective Study

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Abstract

Background: Cardiovascular diseases (CVDs) continue to be the primary cause of death globally, significantly contributing to health deterioration and increased healthcare expenses. Annually, CVDs are responsible for more deaths than any other disease, causing approximately 17.9 million deaths, which equates to around 31% of global mortality. This study investigated the efficacy of high sensitivity c- reactive protein (hs-CRP), Lipoprotein A levels (Lipo A), and Troponin I (Trop I) levels in predicting CVD severity on coronary angiogram

Materials and Methods: This prospective observational study included 211 patients aged 18 years and above, with a diagnosis of acute coronary syndrome (ACS), who visited the Department of Cardiology. A detailed history was recorded, and laboratory investigations included hs-CRP, Lipo A, Trop I, and Lipid Profile, and all the patients were subjected to coronary angiography. Coronary angiogram was studied and the severity of CVD was noted, based on SYNTAX I and II.

Results: The mean age of study patients was 62.82±10.17 years, with age ranging from 34 to 89 years, and the majority being male (70.1%). 78.7% of patients were hypertensive and 71.6% were diabetic. Most common signs and symptoms were chest pain (96.2%) and dyspnoea (87.2%). The higher levels of mean hs-CRP, Lipo A, Trop I, and LDL were significantly associated with the severity of CVD on coronary angiogram ($p<0.001$).

Conclusion: Higher levels of hs- CRP, Lipo A, and Trop I can be a reliable predictor of the severity of CVD on coronary angiogram.

Keywords: Coronary angiogram; coronary artery disease, high-sensitivity C-reactive protein

Introduction

Cardiovascular diseases (CVDs) are the leading global cause of death, significantly affecting health and increasing healthcare costs [1,2]. Non-communicable diseases, including cerebrovascular diseases and coronary heart diseases (CHD), contribute greatly to worldwide mortality, with CVDs accounting for approximately 17.9 million deaths annually, or about 31% of global mortality [3]. India, in particular, has a high burden of these diseases, especially among younger populations [4]. CHD alone caused 7.3 million deaths, while strokes resulted in 6.2 million deaths [5]. By 2030, around 23.6 million deaths from CVDs are expected, primarily due to strokes and

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CHD [3]. Individuals with stable coronary artery disease (CAD) are at a higher risk for recurrent events and mortality, underscoring the need for preventive strategies and intensive management of cardiovascular (CV) risk factors. Concerns specific to India include early onset, rapid progression, and high mortality rates associated with CAD, which cannot be fully explained by conventional risk factors [4].

Cardiac biomarkers are key bio-molecular components in blood that indicate heart damage or stress when released [6]. These biomarkers are crucial for diagnosing and monitoring CVD, thus helping to reduce mortality rates [7]. Circulating biomarkers such as high-sensitivity C-reactive protein (hs-CRP) and cardiac troponin are vital for diagnosing, risk stratifying, and managing conditions like acute coronary syndrome (ACS) and heart failure (HF) [8,9]. Lipoprotein A (Lipo A), a plasma lipoprotein linked to coronary atherosclerosis, has proatherogenic, proinflammatory, and prothrombotic properties [10]. It is emerging as a risk factor for atherosclerotic CVD, potentially influencing patient outcomes independently of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels [11,12]. Limited studies have assessed the efficacy of hs-CRP, Lipo A, and Trop I in evaluating cardiovascular risk in this part of the country. This study aimed to explore the correlation between hs-CRP, Lipo A, and Trop I levels with the severity of CVD on coronary angiogram.

Materials and Methods

This prospective observational study was conducted in the Department of Cardiology from January 2023 to June 2024 after obtaining approval from the Institutional Ethics Committee. The study included 211 patients aged 18 years and above, with a diagnosis of ACS according to the fourth universal definition of acute myocardial infarction [13]. Patients with previous ischemic heart disease who had undergone coronary revascularisation procedure and who returned to undergo coronary angiogram and those who lost to follow-up were excluded from the study. Written informed consent was obtained from each patient prior to their enrolment in the study. Detailed history of the patient was recorded in pre-designed proforma including demographic characteristics and clinical evaluation. Laboratory investigations including hs-CRP, Lipo A, Trop I, Lipid Profile, and HbA1c were done. The hs-CRP level of <1mg/L was considered low; level 1-3 mg/L was considered moderate and level >3mg/L was considered as high in this study [14]. Lipo A level of <30 mg/dL was considered low; 30-50 mg/dL was considered moderate, and above 50 mg/dL was considered high in this study [15]. A level of Trop I below 0.04 ng/mL was considered normal; Troponin I level between 0.04 and 0.39 ng/mL was considered borderline; and a level >0.40 ng/mL was considered high in this study [13]. All study patients were subjected to electrocardiography, echocardiography, and coronary angiography. Coronary angiogram was done using Philips Azurion 5 and Azurion 7 CT machines with Philips QCA analysis capability. A minimum of two views for the right coronary artery and four for the left coronary artery were taken. Additional views were taken if required to distinctly observe the vessel. Coronary angiogram was studied and severity of cardiovascular disease was noted, based on SYNTAX I and II.

Statistical Analysis

Statistical Analysis was performed with the help of Epi Info (TM) 7.2.2.2 EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (χ^2) test was performed to find the associations. t-test was used to compare the means of the two groups. The odds ratio (OR) with a 95% confidence interval was calculated to find the risk factors. Pearson's correlation was done to check the correlation between CVD severity and various study parameters. $p<0.05$ was taken to be statistically significant. SYNTAX 1 score >32 was considered as "High risk", 23-32 was considered "Intermediate risk", and <32 was considered "Low risk" in this study.

Results

In our study, 205 patients demonstrated high SYNTAX scores, while 6 patients had intermediate SYNTAX scores. The overall mean age of study patients was 62.82±10.17 years, with a median age of 62 years and age ranging from 34 to 89 years. The majority of patients (70.1%) were male, overweight (27.5%), and obese (40.3%) with a mean BMI of 25.29±3.33 kg/m^2, and a range was 19-36. Of 211 patients, 147 patients were diabetic and 160 were hypertensive ($p<0.001$). Habit of tobacco was reported in more than half of the study population. Chest pain (96.1%) and dyspnoea (87.3%) were observed in most of the patients in both high-risk and low-risk groups (Table 1). A raised hs-CRP level was observed in 153 patients, a raised Lipo A level was observed in 124 patients, and a Raised Trop I level was observed in 138 patients ($p<0.001$) (Table 2). The majority of our study patients demonstrated lower HDL levels (58.3%) and higher LDL levels (54.5%). Mean HbA1c was 7.51±1.96, median HbA1c was 7.1, and range was 4.7-13.6. The most commonly observed ECG finding was anterior wall STEMI (28.4%), and ST-T changes were observed in all the study patients except one ($p<0.0001$). On Echocardiography, reduced EF was observed in overall 155 study patients (73.5%) ($p<0.0001$). A significant positive correlation of SYNTAX-1 was found with hs-CRP, Lipo A, Trop I, and LDL in this study. Thus, SYNTAX-1 increased with the increasing values of hs-CRP, Lipo A, Trop I, and LDL. However, significant negative correlation was found between SYNTAX-1 and HDL. Thus, SYNTAX-1 increased with the decreasing values of HDL (Table 3, Figure 1).

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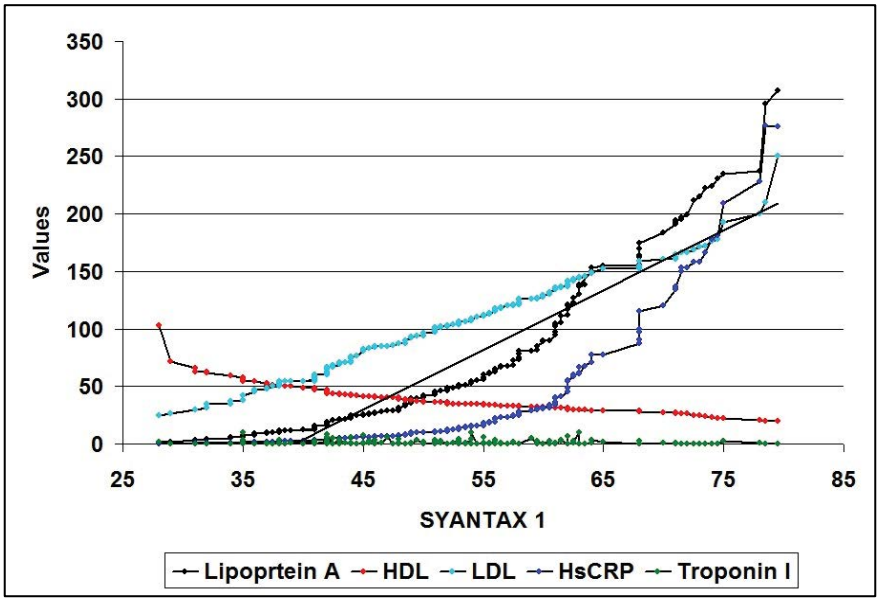

Figure 1: Correlation of SYNTAX 1 with HDL, Hs-CRP, Lipoprotein A, Troponin I, and LDL.

Table 1: Characteristics of Patients in Study Patients.

Patient Characteristics		High risk	Intermediate risk	Total	p-value
		N=205 (%)	N=6 (%)	N=211 (%)	
Age (years)	<50	17 (8.3%)	0 (0.0%)	17 (8.1%)	<0.001
	≥50	188 (91.7%)	6 (100.0%)	194 (91.9%)	
	Total	205 (100.0%)	6 (100.0%)	211 (100.0%)	
	Mean	62.84±10.17	62.17±11.00	62.82±10.17	
Gender	Male	147 (71.7%)	1 (16.7%)	148 (70.1%)	0.014
	Female	58 (28.3%)	5 (83.3%)	63 (29.9%)	
BMI (kg/m²)	Morbid Obese	20 (9.8%)	1 (16.7%)	21 (10.0%)	<0.001
	Obese	82 (40.0%)	3 (50.0%)	85 (40.3%)	
	Overweight	56 (27.3%)	2 (33.3%)	58 (27.5%)	
	Normal	47 (22.9%)	0 (0.0%)	47 (22.3%)	
Diabetes mellitus		147 (71.7%)	4 (66.7%)	151 (71.6%)	
Hypertension		160 (78.0%)	6 (100.0%)	166 (78.7%)	
Tobacco Habit		113 (55.12%)	0 (0.0%)	113 (46.4%)	
Alcohol Habit		33 (16.1%)	0 (0.0%)	33 (15.6%)	
Presenting Complaints	Chest Pain	197 (96.1%)	6 (100.0%)	203 (96.2%)	<0.001
	Dyspnoea	179 (87.3%)	5 (83.3%)	184 (87.2%)	
	Syncope	2 (1.0%)	0 (0.0%)	2 (0.9%)	
	Palpitation	6 (2.9%)	0 (0.0%)	6 (2.8%)	
	Angina equivalents	3 (1.5%)	0 (0.0%)	3 (1.4%)	
Pulse rate (beats/ minute)	Bradycardia	4 (2.0%)	0 (0.0%)	4 (1.9%)	<0.001
	Normal	197 (96.1%)	6 (100.0%)	203 (96.2%)	
	Tachycardia	4 (2.0%)	0 (0.0%)	4 (1.9%)	
Blood Pressure	High	145 (70.7%)	5 (83.3%)	150 (71.1%)	<0.001
	Normal	60 (29.3%)	1 (16.7%)	61 (28.9%)	

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Table 2: Comparison of Study Parameters in Patients.

Study Parameters		High risk	Intermediate risk	Total
		N=205 (%)	N=6 (%)	N=211 (%)
hs-CRP	High	149 (72.7%)	4 (66.7%)	153 (72.5%)
	Normal	56 (27.3%)	2 (33.3%)	58 (27.5%)
	Mean	29.93±59.14		
Lipoprotein A	High	123 (60.0%)	1 (16.7%)	124 (58.8%)
	Normal	82 (40.0%)	5 (83.3%)	87 (41.2%)
	Mean	60.32±60.53		
Troponin I	High	134 (65.36%)	4 (66.7%)	138 (65.40%)
	Normal	71 (34.6%)	2 (33.3%)	73 (34.6%)
	Mean	1.03±1.85		
HbA1c Level	Normal	35 (17.1%)	1 (16.7%)	36 (17.1%)
	Pre-diabetic	43 (21.0%)	1 (16.7%)	44 (20.8%)
	Diabetic	127 (62.0%)	4 (66.7%)	131 (62.1%)
	Mean	7.51±1.96		
HDL level	Below the normal	121 (59.0%)	2 (33.3%)	123 (58.3%)
	Normal	84 (41.0%)	4 (66.7%)	88 (41.7%)
	Mean	39.13±10.14		
LDL level	High	114 (55.6%)	1 (16.7%)	115 (54.5%)
	Normal	91 (44.4%)	5 (83.3%)	96 (45.5%)
	Mean	97.93±39.33		

Table 3: Correlation between SYNTAX-1 with different parameters.

	hs-CRP	Lipo A	Trop I	HDL	LDL
Pearson Correlation (r)	0.732	0.932	0.831	-0.911	0.993
p-value	<0.0001*	<0.0001*	<0.0001*	<0.0001*	<0.0001*

Discussion

Inflammation is a key factor in the development of arterial hypertension, heart failure, valvular disease, and atrial fibrillation [16]. Due to the challenges of assessing vascular inflammation through cardiac imaging, testing for inflammatory biomarkers in peripheral blood is becoming increasingly important. We studied the correlation of hs-CRP, Lipo A, and Trop I levels with angiographic severity of CVD. The mean age of patients with ACS in our study was 62.82±10.17 years, with the majority being above 50 years of age (91.9%) among both high-risk and intermediate-risk groups. (Table 1) These findings are in accordance with previous studies [17-21]. Similar to our study, male dominance among patients with CVD was observed in the other studies [17-20,22]. The mean BMI of ACS patients in our study was 25.29±3.33kg/m^2, with the majority being in overweight and obese categories (77.8%), similar to the study by Silverio et al. [10]. 78.7% of patients were hypertensive and 71.6% of patients were known cases of Type 2 Diabetes Mellitus (T2DM) (p<0.001) in our study. These observations were in accordance with previous studies [10,19,20,22]. Our study suggested that advanced age (≥50 years), male gender, high BMI, hypertension, and T2DM are risk factors for CVD severity in this study population (p<0.0001).

In our study, all the patients with the habit of tobacco use and alcohol consumption were in the high-risk group, suggesting a significant correlation between tobacco habit and higher risk of CVD severity. Chest pain (96.2%) and dyspnoea (87.2%) were commonly observed in our study patients (p<0.001), as evident from previous studies [21]. These findings were observed in both high-risk and intermediate-risk groups. Although there was no significant association of pulse rate (p=0.88) with risk of CVD severity, high BP was significantly associated with high and intermediate risk of CVD severity in our study.

In ACS patients, hs-CRP levels commonly exceed 10 mg/L and can reach up to 30–50 mg/L or higher in severe cases [23-25]. One study observed that hs-CRP levels were as high as >50 mg/L in some ACS patients, particularly those with extensive myocardial damage [26]. In our study, the mean hs-CRP level was 29.93±59.14, the median hs-CRP level was 9.8, with a range from 0.2-576 (Table 2). As there were some outliers, the mean hs-CRP level could not be taken as an average, as it would be affected by skewed values, hence median was taken as average in our study. Among the high-risk and intermediate-risk group patients, hs-CRP was raised in 72.7% and 66.7% of patients, respectively, suggesting a positive correlation between raised hs-CRP level and risk of

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CVD severity in the study population. In our study, it was observed that the severity of CVD was 1.33 times higher in patients with raised hs-CRP levels than those with normal levels. High Lipo A levels were observed in 60% of patients in the high-risk group, while in the intermediate group, only 16.7% of patients demonstrated high Lipo A levels, suggesting a significant correlation between raised Lipo A levels with high-risk of CVD severity in our study ($p<0.001$). Similar observations were made in a recent study from UAE [27]. However, in contrast to our results, one recent study from Karnataka, India has not observed any significant association between Lipo A and angiographic severity of CAD in their study [28]. Our study showed that CAD patients with higher Lipo A levels are at 7.5 times higher risk of having angiographic CVD severity than those with normal Lipo A levels.

In our study, Trop I level was high in 65.36% of patients in the high-risk group, and 66.7% of patients in the intermediate-risk group, suggesting a significantly positive correlation between Trop I level and angiographic severity of CVD ($p<0.001$), similar to a recent study from Denmark [21]. Our study showed that patients with lower HDL levels are at 2.88 times higher risk of having severe CVD than those with normal levels of HDL. In our study, a total of 55.6% of patients in the high-risk group had higher LDL levels, which were significantly higher than those with normal LDL levels ($p=0.04$), suggesting a significant correlation between LDL levels and angiographic severity of CVD. In our study, there was a statistically significant association between ST-T changes in ECG and reduced EF with the risk of CVD severity ($p<0.0001$). Our study showed that the risk of CVD severity was 2.86 times higher in patients with reduced EF than the patients with normal EF.

ST-T changes were observed in all the study patients except one, suggesting a statistically significant association between ST-T changes on ECG and with risk of CVD severity ($p<0.0001$). 74.1% of patients in the high-risk group had reduced EF, suggesting a statistically significant association between EF and the severity of CVD. Our study showed that the risk of CVD severity was 2.86 times higher in patients with reduced EF than in patients with normal EF. The mean SYNTAX 1 score in our study was 50.86±10.85. A significant positive correlation of SYNTAX-1 was found with hs-CRP, Lipo A, Trop I, and LDL in this study, whereas a significant negative correlation was found between SYNTAX-1 and HDL. Thus, SYNTAX-1 increased with the decreasing values of HDL. Being a single-center study was one limitation of this study. Though the correlation with the SYNTAX score is positive in this study, the study does not include long-term outcomes (e.g., survival, MI recurrence), limiting its predictive value for future events.

Conclusion

This study showed that advanced age, male gender, obesity (high BMI), hypertension, and T2DM were risk factors for the angiographic severity of CVD. The higher levels of mean hs-CRP, Lipo A, and Trop I levels were significantly associated with severe CVD on coronary angiograms in our study. Additionally, lower HDL levels and higher LDL levels were also significantly associated with angiographic severity of CVD. Thus, this study concluded that hs-CRP, Lipo A, and Trop I levels, in addition to HDL and LDL levels, are reliable predictors of CVD severity in patients with ACS.

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